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Cryst.Struct.Comm. (1972). 1, 71.

DL-N-t-BUTYL-2(4-HYDROXY-3-HYDROXYMETHYLPHENYL)2-HYDROXYETHYLAMINE, (SALBUTAMOL, Ah.3365), $C_{13}H_{21}NO_3$

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Introduction. The crystal structure of Salbutamol has been determined by X-ray diffraction. Salbutamol is one compound of a new series of β-adrenergic stimulants which have been found to have considerably greater action on bronchial smooth muscle than on other smooth muscle affected by β-stimulants, and is currently being used in many countries for the treatment and management of asthma (Hartley, Jack, Lunts and Ritchie, 1968; Brittain, Farmer, Jack, Martin and Simpson, 1968).

Crystal Data. Rectangular crystals were obtained by recrystallisation from water. The space group as determined from systematic spectral absences is Pbca; the unit cell dimensions are : a = 21.654(10), b = 8.798(4), c = 14.565(7) Å; Z = 8; ρ_{obs} = 1.15 g cm^{-3}, ρ_{calc} = 1.15 g cm^{-3}.

Data Collection, Structure Elucidation and Refinement. A total of 2644 independent reflections were measured on a Siemens automatic single crystal diffractometer using CuKα radiation and nickel attenuators (Craig, 1971). The structure was solved using direct phasing procedures incorporating programmes NORM, PHREL and GSAM written by Grainger. Reflections having $|E_{obs}| \geq 1.60$ (272 in number) were selected and used in the phase analysis and calculation of an E map from which the positions of all non-hydrogen atoms were obtained. Eventually all atoms (including hydrogens) were located and the structure refined by full matrix least squares procedures to an overall discrepancy (R) factor of 0.048. It is worth noting that comparison between the fully refined phases of the initial 272 selected reflections and those used to phase the E map revealed that only one phase was incorrectly assigned in the first instance.

Atomic Co-ordinates

	x/a(σ)	y/b(σ)	z/c(σ)		x/a(σ)	y/b(σ)	z/c(σ)
O(1)	0.3281(1)	0.5307(2)	0.2241(1)	H(3)	0.314(1)	0.557(3)	0.169(2)
O(2)	0.3341(1)	0.4496(2)	0.5016(1)	H(4)	0.315(1)	0.397(3)	0.373(2)
O(3)	0.2849(1)	0.9869(1)	0.5541(1)	H(5)	0.389(1)	0.425(3)	0.390(2)
C(1)	0.3217(1)	0.8932(2)	0.4060(1)	H(6)	0.347(1)	0.350(3)	0.519(2)
C(2)	0.3127(1)	0.9193(2)	0.3132(1)	H(7)	0.337(1)	0.720(3)	0.501(2)
C(3)	0.3145(1)	0.8002(2)	0.2510(1)	H(8)	0.303(1)	1.117(3)	0.445(2)
C(4)	0.3255(1)	0.6537(2)	0.2815(1)	H(9)	0.242(1)	0.974(3)	0.536(2)
C(5)	0.3343(1)	0.6241(2)	0.3748(1)	H(10)	0.402(1)	0.963(3)	0.535(2)
C(6)	0.3323(1)	0.7455(2)	0.4358(1)	H(11)	0.411(1)	1.082(3)	0.453(2)
C(7)	0.3206(1)	1.0240(2)	0.4744(1)	H(12)	0.357(1)	1.162(3)	0.620(2)
C(8)	0.3853(1)	1.0616(2)	0.5071(2)	H(13)	0.417(1)	1.433(3)	0.650(2)
N	0.3852(1)	1.1903(2)	0.5708(1)	H(14)	0.472(1)	1.365(3)	0.710(2)
C(9)	0.4464(1)	1.2314(2)	0.6115(2)	H(15)	0.408(2)	1.327(4)	0.729(2)
C(10)	0.4331(2)	1.3530(5)	0.6815(3)	H(16)	0.486(1)	1.012(3)	0.619(2)
C(11)	0.4779(1)	1.0981(3)	0.6584(2)	H(17)	0.518(1)	1.132(3)	0.679(2)
C(12)	0.4877(1)	1.2927(4)	0.5357(3)	H(18)	0.455(1)	1.043(3)	0.707(2)
C(13)	0.3445(1)	0.4625(2)	0.4056(1)	H(19)	0.471(1)	1.375(3)	0.503(2)
H(1)	0.305(1)	1.024(3)	0.291(2)	H(20)	0.525(1)	1.317(3)	0.552(2)
H(2)	0.311(1)	0.819(3)	0.187(2)	H(21)	0.503(1)	1.211(3)	0.473(2)

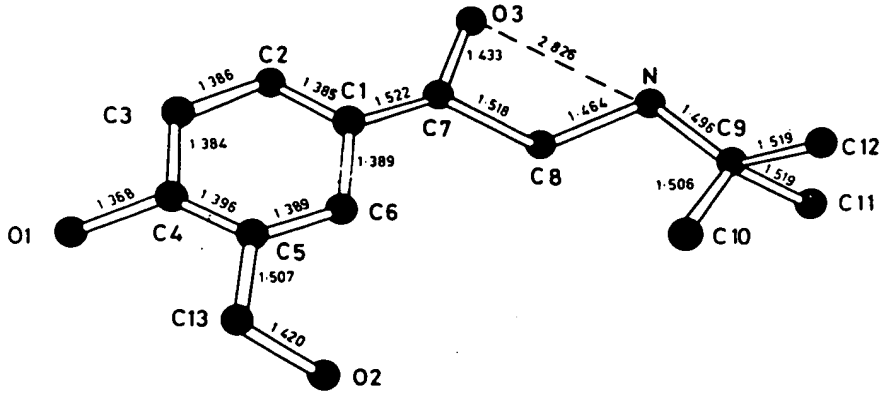

Fig.1. A diagram of a molecule of Salbutamol showing some intramolecular bond distances.

Bond Distances and Angles

O(1)-C(4)	1.368(2) Å	C(6)-C(1)	1.389(3) Å
O(2)-C(13)	1.420(2)	C(1)-C(7)	1.522(2)
O(3)-C(7)	1.433(2)	C(7)-C(8)	1.518(3)
C(1)-C(2)	1.385(3)	C(8)-N	1.464(2)
C(2)-C(3)	1.386(3)	N-C(9)	1.496(2)
C(3)-C(4)	1.384(3)	C(9)-C(10)	1.506(4)
C(4)-C(5)	1.396(3)	C(9)-C(11)	1.519(3)
C(5)-C(13)	1.507(3)	C(9)-C(12)	1.519(4)
C(5)-C(6)	1.389(2)		

O(1)-C(4)-C(3)	123.2(2)°	C(6)-C(1)-C(2)	118.9(2)°
O(1)-C(4)-C(5)	116.2(2)	C(6)-C(1)-C(7)	120.4(2)
O(2)-C(13)-C(5)	110.2(2)	C(2)-C(1)-C(7)	120.7(2)
C(13)-C(5)-C(4)	119.0(2)	C(1)-C(7)-C(8)	110.8(1)
C(13)-C(5)-C(6)	122.6(2)	C(7)-C(8)-N	111.5(2)
O(3)-C(7)-C(1)	111.5(1)	C(8)-N-C(9)	115.9(1)
O(3)-C(7)-C(8)	107.0(2)	N-C(9)-C(10)	105.6(2)
C(1)-C(2)-C(3)	120.6(2)	N-C(9)-C(11)	112.9(2)
C(2)-C(3)-C(4)	119.9(2)	N-C(9)-C(12)	108.6(1)
C(3)-C(4)-C(5)	120.6(2)	C(10)-C(9)-C(11)	109.3(2)
C(4)-C(5)-C(6)	118.3(2)	C(10)-C(9)-C(12)	110.7(3)
C(5)-C(6)-C(1)	121.6(2)	C(11)-C(9)-C(12)	109.7(2)

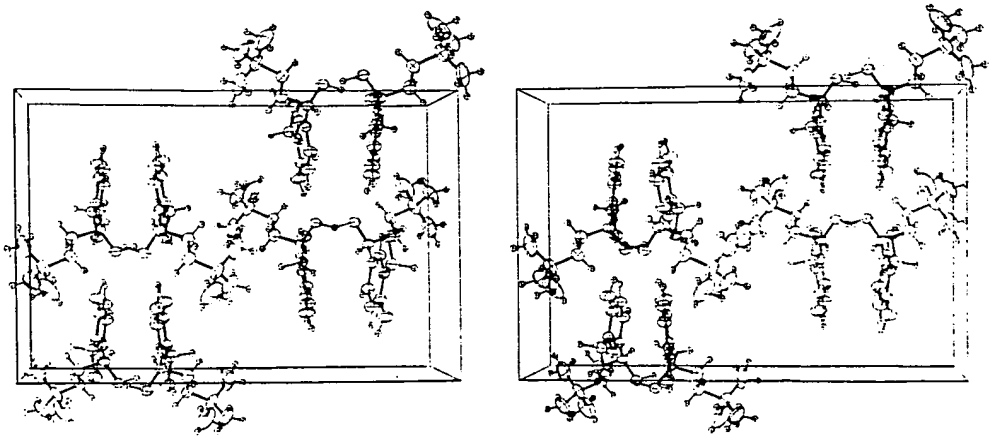

Fig.2. A packing diagram showing the unit cell contents of Salbutamol.

Comments. Salbutamol exhibits the same cis orientation of amino and hydroxyl groups as observed with Th1165 (Beale, 1972). The N...O distance (2.826(2) Å) is in fact a little larger than the corresponding distance (2.766(3) Å) in Th1165. The benzene ring is inclined at 74.5(2)° to the

plane of the C(7)-C(8)-N-C(9) atoms, whilst in the Th1165 molecule this angle is 66.9(3)°. The tertiary butyl group is on the opposite side of the Salbutamol molecule to the amino and hydroxyl groups. The Th1165 molecule has the substituent groups on the nitrogen atom on the same side of the molecule as the amino and hydroxyl groups and therefore in closer proximity to the receptor site.

Acknowledgments. The authors are indebted to the Asthma Foundation of New South Wales for the award of a post-doctoral research Fellowship to one of us (JPB). We are also grateful to Associate Professor N.C.Stephenson for his continued interest and help, to Professor W.F.Glover and Dr.S.McLean, School of Physiology, The University of New South Wales for their assistance. We would also like to thank Professor M.M.Woolfson,Dr.P.Main (York University, England) and Dr.G.Germain (Louvain University, Belgium) for supplying us with LSAM. Finally, we would like to express our thanks to Glaxo-Allenburys (Aust.) Pty. Limited for samples of Salbutamol.

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Received: 4 January 1972

VOL. 1 - No 1 - 1 JANUARY 1972

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